



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0083]

Draft Guidance for Industry on Heparin for Drug and Medical Device Use; Monitoring Crude Heparin for Quality; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality.” This draft guidance is intended to alert manufacturers of active pharmaceutical ingredients (APIs), pharmaceutical and medical device manufacturers of finished products, and others to the potential risk of crude heparin contamination.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT:

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#### SUPPLEMENTARY INFORMATION:

##### I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality.” This draft guidance provides recommendations that will help API manufacturers, pharmaceutical and medical device manufacturers of finished products, and others, to better control their use of crude heparin that might contain oversulfated chondroitin sulfate (OSCS) or non-porcine material (especially ruminant material) contaminants. This draft guidance on crude heparin recommends strategies to test for contamination and should be used in addition to the United States Pharmacopeia (USP) monograph testing required for other forms of heparin to detect the presence of OSCS.

Following reports of serious adverse events (including deaths) among patients injected with heparin sodium in 2008, FDA identified the contaminant OSCS in heparin API manufactured in China. FDA is also concerned about the potential for contamination of heparin with the bovine spongiform encephalopathy (BSE) agent derived from ruminant materials. The control of the quality of crude heparin is critical to ensure the safety of drugs and devices and to protect public health. FDA developed this draft guidance to alert manufacturers to the risks of crude heparin contaminants and to recommend strategies to ensure that the heparin supply chain

is not contaminated with OSCS or any non-porcine origin material, especially ruminant material (unless specifically approved or cleared as part of drug or medical device application).

The draft guidance recommends that manufacturers test and confirm the species origin of crude heparin in each shipment before use in the manufacture or preparation of a drug or medical device containing heparin. The test method should be qualified for use in testing crude heparin and for the identification of species origin. The method should be based on good scientific principles (e.g., sufficient accuracy and specificity) and possess a level of sensitivity commensurate with the current state of scientific knowledge and risk. Likewise, the draft guidance recommends that manufacturers test for OSCS in crude heparin in each shipment before use, using a qualified test method that is suitable for detecting low levels of OSCS concentrations and is based on good scientific principles. Manufacturers should reject for use and control or destroy crude heparin found to contain any amount of OSCS and notify FDA of any such finding. The draft guidance also recommends that manufacturers identify and audit crude heparin suppliers and heparin API suppliers to ensure conformance to current good manufacturing practice (CGMP), employ the controls described in the guidance for industry “Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients,” and comply with the quality system regulations (as applicable).

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency’s current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

## II. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

### III. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). In the draft guidance, FDA advises drug and medical device manufacturers who receive and use crude heparin to manufacture drugs and medical devices to notify the Agency of crude heparin found to contain any amount of OSCS (for human drugs 21 CFR 314.81(b)(1)(ii); for animal drugs 21 CFR 514.80(b); for medical devices 21 CFR 803.50). The collections of information in 21 CFR 314.81(b)(1)(ii) have been approved under OMB control number 0910-0001; in 21 CFR 514.80(b) under OMB control number 0910-0284; and in 21 CFR 803.50 under OMB control number 0910-0437.

### IV. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, <http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm>,

<http://www.fda.gov/MedicalDvices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>, or <http://www.regulations.gov>.

Dated: February 8, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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